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1 Original Article

5 **High resolution exposure modelling of heat and air pollution and the impact**

6 **on mortality**

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35 <u>Running title</u>

36 Heat, air pollution and mortality

1   **Abstract (201 words)**

2

3   **Background**: Elevated temperature and air pollution have been associated with increased

4   mortality. Exposure to heat and air pollution, as well as the density of vulnerable groups

5   varies within cities. The objective was to investigate the extent of neighbourhood differences

6   in mortality risk due to heat and air pollution in a city with a temperate maritime climate.

7   **Methods**: A case-crossover design was used to study associations between heat, air

8   pollution and mortality. Different thermal indicators and air pollutants (PM_{10}, NO_2, O_3) were

9   reconstructed at high spatial resolution to improve exposure classification. Daily exposures

10   were linked to individual mortality cases over a 15 year period.

11   **Results**: Significant interaction between maximum air temperature (Ta_{max}) and PM_{10} was

12   observed. During "summer smog" days ($Ta_{max} > 25$ ºC and $PM_{10} > 50$ µg/m^3), the mortality

13   risk at lag 2 was 7% higher compared to the reference (Ta_{max} 15 °C and PM_{10} 15 µg/m^3).

14   Persons above age 85 living alone were at highest risk.

15   **Conclusion**: We found significant synergistic effects of high temperatures and air pollution

16   on mortality. Single living elderly were the most vulnerable group. Due to spatial differences

17   in temperature and air pollution, mortality risks varied substantially between

18   neighbourhoods, with a difference up to 7%.

19   <u>Key words</u>

20   heat stress, air pollution, mortality, case-crossover study, vulnerable groups, spatial variation

28

| 1 | **1. Introduction** |

2   Elevated temperatures are associated with increased mortality,[1-5] with air pollution acting as

3   a confounder or effect modifier.[3,6,7] However, the threshold and severity of heat effects

4   varies by country and latitude, which can be explained by differences in various physiological

5   as well as behavioural factors.[5,8] Examples of these factors are acclimatisation to hot

6   weather and the ability to thermoregulate the body, as well as time spent indoors, and the

7   use of air conditioning.[4] These factors may also differ within a population, which makes

8   certain subgroups more susceptible to heat effects than others.[1,3,9,10]

9   Regarding heat exposure it is known that urban areas typically have higher temperatures

10 than suburban or surrounding areas, a phenomenon known as the Urban Heat Island (UHI)

11 effect.[11] The UHI effect is influenced by urban characteristics such as building height,

12 material and orientation as well as the amount of green space and water, which all vary

13 between urban areas. Generally, the dry and dark urban surfaces will become hotter

14 compared to lighter, moist or shaded surfaces because of easier absorption of sunlight. [12]

15 Besides differences in heat exposure, there are also differences in exposure to air pollution,

16 and density of potentially vulnerable groups within a city. Hence, substantial differences in

17 heat-mortality risks between urban neighbourhoods are expected.

18 The objective and novelty of this study was to investigate the extent of effect modification

19 between heat and air pollution, and if spatial differences in exposure within a city lead to

20 discernible differences in mortality risk between neighbourhoods. This was done using

21 thermal, air pollution and mortality data on the city of Rotterdam, a Dutch city with a

22 maritime temperate climate and a multi-ethnic and socioeconomic diverse population. We

23 used a case-crossover design in combination with high resolution exposure modeling to

24 calculate associations and to examine possible interactions between heat, air pollution and

25 natural-cause mortality. We also investigated if certain subgroups, determined by sex, age,

26 ethnicity, marital status and household income, were more susceptible to heat-related

27 mortality than the urban population as a whole.

28

1 **2. Material and methods**

2 2.1. <u>Study population</u>

3 The associations between heat, air pollution and mortality were studied in Rotterdam over

4 the period 1995-2009. Rotterdam is a city with around 600.000 inhabitants in the

5 Netherlands, located in Northern Europe close to the North Sea, and therefore benefits from

6 relatively cool and clean sea breezes. Rotterdam consists of 90 neighbourhoods with an

7 average size of 2.3 km^2, and has a large port and industrial area.

8 The study population consisted of natural-cause mortality cases in Rotterdam during this

9 period, which were retrieved from the mortality database of Statistics Netherlands (in Dutch:

10 Centraal Bureau voor de Statistiek (CBS)). Natural-cause mortality cases were selected

11 according to the International Classification of Disease (ICD) codes 9th (for the year 1995)

12 and 10th revision (1996-2009), excluding death due to all external causes such as accidents,

13 suicides, poisoning etc. Information about age, sex, marital status, ethnicity and household

14 income (defined as a standardised measure for the prosperity of a household and corrected

15 for differences in household size and composition)[13] of these cases were available from the

16 same database. This database is protected by strict privacy regulations, so the analysed data

17 were completely anonymous. The Dutch Code of Conduct for Medical Research allows the

18 use of anonymous data for research purposes without an explicit informed consent.[14]

19 Daily, neighbourhood specific exposure data on heat and air pollution for the study period

20 were merged to the mortality dataset, and matched by neighbourhood of residence and

21 date of death of the cases in our study. Exposure was averaged on neighbourhood level

22 because the exact home addresses of the mortality cases were not accessible due to privacy

23 regulations.

24 2.2. <u>Heat exposure assessment</u>

25 Besides temperature, other meteorological factors such as humidity, wind speed and solar

26 radiation, are also important in determining the outdoor thermal environment. Therefore,

27 daily exposure to heat was assessed using three indices: daily maximum air temperature

28 (Ta), mean radiant temperature (Tmrt),[15,16] and the Universal Thermal Comfort Index

29 (UTCI).[16]

Tmrt is a parameter that influences the energy balance and thermal comfort (heat load) of humans, and therefore useful when assessing the impact of heat on people's health.[15] Tmrt is directly influenced by urban geometry and surface material, and therefore also a good measure to identify urban hot spots. Tmrt can be calculated from the total radiation flux density absorbed by the body, which is the sum of all short- and longwave radiation fluxes (both direct and reflected) to which a human body is exposed, the emissivity of the human body, and the Stefan-Boltzmann constant according to the Stefan-Boltzmann law formulas described in the paper of Thorsson et al.[15] Total radiation flux densities can be modelled using inputs of global shortwave radiation, air temperature and relative humidity.[16]

The UTCI is an indicator sensitive to changes in radiation, humidity and wind speed in both cold and warm conditions, and is often applied in public weather services, public health services, urban planning and design.[17]

Meteorological data were retrieved from the Royal Netherlands Meteorological Institute (KNMI) station at Rotterdam Airport, located north of Rotterdam (approximately 3 km distance from city centre). Air temperature, relative humidity, wind speed and global radiation were used as input for the models that constructed the various daily heat indices for the different neighbourhoods in Rotterdam during the study period.

Neighbourhood-specific daily air temperature was modelled according to the method of Klok et al.[17] The Urban Heat Island effect in the city centre of Rotterdam (UHI_city centre) was estimated as the annual mean difference in air temperature between a weather station in the city centre (near Central Station) and Rotterdam Airport. This was found to be 1.2 °C. Differences in the surface temperature (Ts) between each neighbourhood and the airport and city centre (derived from satellite images) were used to scale this 1.2 °C to UHI effect values for each neighbourhood.[18] Hourly air temperatures measured at Rotterdam Airport (Ta_airport) were corrected with this value to calculate hourly air temperatures for each neighbourhood (Ta_neighb). From this we could retrieve neighbourhood-specific daily maximum air temperatures (Ta_{max}) during the study period.

Neighbourhood-specific daily Tmrt and UTCI were both calculated using the SOLWEIG 1D (Solar and Longwave Environmental Irradiance Geometry) model.[15,19] Technical details of the exposure assessment using this model are descibred in the online supplement.

1 2.3.   Air pollution exposure assessment

2 Daily exposure to particulate matter with a diameter of ≤10 µm (PM_{10}), nitrogen dioxide

3 (NO_2) and ozone (O_3) were estimated for the study period, using dispersion modelling in

4 combination with air quality measurements.[20] Because home addresses were not available,

5 we determined daily population weighted average (PWA) concentrations per neighbourhood

6 instead. These were calculated from the daily average concentrations for three different

7 'exposure situations' in each neighbourhood and calibrated with daily measurement data.

8 These 'exposure situations' were: streets with more than 10,000 vehicles per day (Zone 1),

9 areas up to 100 m from urban motorways (Zone 2) and the rest of the urban area in a

10 neighbourhood (Zone 3). Subsequently, the PWA concentration for a given neighbourhood

11 was computed taking into account the number of people (#) living in each of these zones:

12

13 PWA ($µg/m^3$)= ((C*#)Zone 1+(C*#)Zone 2+(C*#)Zone 3) / (#Zone 1+#Zone 2+#Zone 3)   (1)

14

15 with C the daily average concentration of a pollutant in $µg/m^3$ in each zone per

16 neighbourhood.

17

18 Concentrations of PM_{10}, NO_2 and O_3 for Zone 3 in a neighbourhood were derived from

19 background concentrations at 1*1 km spatial resolution grids. These background

20 concentrations are based on a combination of modelling and measurements in the National

21 Air Quality Monitoring Network.[21] The contribution of road traffic emissions from streets

22 and motorways is added to the urban background in each neighbourhood (Zone 3

23 concentration) to obtain Zone 1 and 2 concentrations. More details on modelling of the

24 traffic contributions are described in the online supplement.

25 The uncertainty involved in modelling the annual averages of regulated air pollutants at a

26 certain location in the Netherlands has been estimated as 20%.[22] In this study, the modelled

27 daily averages were calibrated by daily measurements and therefore a similar uncertainty is

28 assumed for PM_{10}, NO_2 and O_3.

29 2.4.   Study design and data analysis

30 The case-crossover design was used to assess the relations between heat, air pollution and

31 mortality. This design is a modification of the matched case-control design in which each

case acts as his/her own control, and distribution of exposure is compared between cases and controls. Exposure at the time of event (i.e. case date) is compared with a set of referent (control) dates that represent the expected distribution of exposure for non-event follow-up times.[22-24] This means that the individual mortality cases in our dataset were merged with heat and air pollution exposure in their neighbourhood of residence on the date of death as well as on three referent dates. The case date of a person was defined as the date of death. The three referent dates were selected by the time stratified method,[24-26] which implies that they are matched on day of the week, month and year with the case date of each subject. For example, when a case died on Monday the 6th of May 1996, referent dates were chosen on the 13th, 20th and 27th of May 1996, when a case died on Tuesday the 10th of June 1997, referent days were chosen on the 3rd, 17th and 24th of June 1997 and so on. This method of referent date selection explicitly controls for time trends, seasonality and chronic and slowly varying potential confounders.[24,27] Besides same-day exposures (lag 0), lag times of 1 and 2 days before the date of death, with referent dates chosen accordingly, were also evaluated.

Conditional logistic regression analyses were conducted to calculate odds ratios and corresponding 95% confidence intervals (CIs) associated with thermal exposure. Confounding and effect modification by air pollution were assessed using multivariate models.

It is known that the temperature-mortality association typically follows a U-, V-, or J-shaped curve, with increased mortality below and above a certain threshold, which varies by country or region.[8,28,29] In general, cold effects are delayed and last for many days, while heat effects appear quickly and do not last long.[4,5,30] Confounding or effect modification of cold and heat stress effects on mortality by air pollution may therefore be different, and is probably most efficiently studied by separate models. In this study, we chose to focus on the combination of heat stress and air pollution effects on natural-cause mortality.

One of the options to do this is to split the data in a cold and a warm season (e.g. October-March and April-September). However, the warm season data could have been "contaminated" with days below the threshold value causing attenuation of the heat stress effect, while days above the threshold value in the cold season data are lost. Therefore, we used all-year data with a quadratic (U-shape) term to model heat exposure. The quadratic

term was centered at the average value of the specific heat exposure parameter, functioning as a reference for the increase in risk with increasing heat exposure. We only interpreted the heat-mortality relationship at the right "warm" end of the quadratic term. The air pollution parameters were included in the models as linear terms.

To focus the research, we first analysed univariate associations between all heat and air pollution exposure parameters and mortality. Subsequently, we selected the heat indicator and lag model with the lowest Akaike Information Criterion (AIC), and used the least correlated air pollution parameter to define multivariate and interaction models. Effect modification by air pollution was studied by including an interaction term effective from the threshold value (of the heat parameter) upwards (modelled as a spline with a knot at the threshold value) in the model. Multivariate and interaction models were built only for the selected parameters and lag time to avoid multiple testing, these were Ta_{max} and PM_{10}. We chose PM_{10} over O_3 as pollution indicator, because O_3 was substantially correlated with temperature (Table 2). The multivariate models containing interaction terms between Ta_{max} and PM_{10} revealed significant effect modification of the temperature-mortality relationship by air pollution. Therefore, mortality risks are shown at different combinations of temperature and air pollution levels.

The following formulas describe the calculation of the mortality risks (MR) based on the estimates derived from the different univariate and multivariate conditional regression analyses:

- MR = EXP(B1*Ta_{max} centered + B2*(Ta_{max} centered^2))
- MR = EXP(B1*PM_{10}_IQR)
- MR = EXP(B1*Ta_{max} centered + B2*(Ta_{max} centered^2) + B3*PM_{10}_value +
B4*(PM_{10}_value*Ta_{max} centered$^{\#}$))Where:

Ta_{max} centered = Ta_{max} – 14.27 (the average Ta_{max} value).

PM_{10}_value = the level of PM_{10} for which the mortality risk is calculated.

Ta_{max} centered$^{\#}$ = is 0 when Tamax is below 15 °C.

To investigate the extent of neighbourhood differences in heat-mortality risks, we looked at average differences in heat (Ta_{max}) and air pollution (PM_{10}) between neighbourhoods during

warm days with high pollution (summer smog days), and translated these differences into differences in mortality risk increase.

Susceptible subgroups were identified by stratified analyses based on sex, age (<45, 45-64, 65-84 and ≥85 years), marital status (never married, married, widowed and divorced), ethnicity (Dutch, Western and non-Western origin) and household income quartiles (<14842 €/year, 14842-19850 €/year, 19850-26497 €/year, >26497 €/year). We compared the risk of mortality following "summer smog" days (Ta_{max} 25 ºC and PM_{10} 50 µg/m^3) (lag 2) between the different subgroups in the total population and in the population aged 65 or older.

3. Results

3.1. Study population

The average number of inhabitants in Rotterdam over the period 1995-2009 was ± 600.000 with approximately 5500 to 6000 deaths a year. For this study period, we were able to merge both meteorological and air pollution data to 73,178 mortality cases. Demographic characteristics of these cases and the cases aged ≥65 years are shown in Table 1. Household income data were available from 2003 onwards, for 26,381 cases. In the population aged 65 years or older, there was a larger proportion of people from Dutch origin, and widowed people than in the population as a whole.

3.2. Heat and air pollution exposure

Figure 1 shows the distribution of the various thermal and air pollution exposure indicators during the study period. Table 2 contains correlations between the different exposure parameters. Correlations between the different thermal indicators were substantial (i.e. between 0.75 and 0.95). The correlations between the different air pollution parameters were moderate (i.e. all smaller than 0.5). Finally, correlations between thermal and air pollution parameters were weak (i.e. between -0.22 and -0.02), except for ozone (with Pearson correlation coefficients ranging from 0.63-0.70).

3.3. Univariate associations between heat, air pollution and natural-cause mortality

Table 3 shows the univariate associations between the different heat parameters and mortality at lag 0, 1 and 2 days, while Table 4 shows the univariate associations between air pollution and mortality. The associations are expressed as percentage increase in risk (%)

1   and 95% confidence intervals for the increase between 90% and 99% of the specific thermal

2   index (Table 3), and per iqr increase for the air pollution parameters (Table 4).

3   According to the AIC, Ta_{max} was the best performing thermal indicator at all lag times. Figure

4   2 shows the quadratic curves at different lags for the risk increase with Ta_{max} increasing or

5   decreasing from the average exposure (14.27 ºC).

6   Table 4 shows that according to the AIC, PM_{10} was the best performing air pollution indicator

7   at lag 0 and 2, while O_3 was the best performing indicator at lag 1.

8   3.4.   Interaction between heat and air pollution

9   Figure 3, Figure 4, and Figure 5 show the interaction models at lag 0, 1 and 2 days. The AIC

10   revealed that lag 2 was the best performing model.

11   Table 5 shows the frequency of certain temperature and air quality combinations (when

12    $Ta_{max} \geq 15$ºC) averaged over the total study area. On 2,679 days (48.9% of the total study

13   period) Ta_{max} was 15 ºC or higher. The most frequent combination (27.3% of the days with

14    $Ta_{max} \geq 15$ºC) was a Ta_{max} between 15 and 20 ºC and a PM_{10} level between 15 and 30 µg/m^3

15   (further referred to as "reference" days). The increased risk of natural-cause mortality

16   following these "reference" days lies between 0 and 3% (Figure 5). During 158 days (5.9% of

17   the days with $Ta_{max} \geq 15$ºC) the average Ta_{max} in the area was 25 ºC or higher combined with

18   an average PM_{10} level exceeding the 24 hour limit value of 50 µg/m^3 (further referred to as

19   "summer smog" days). The risk of natural-cause mortality was at least 7% higher after these

20   "summer smog" days (lag 2) compared to the mortality risk following "reference" days

21   (Figure 5).

22   3.5.   Neighbourhood differences in heat-mortality risk

23   During "summer smog" days the maximum difference in Ta_{max} between neighbourhoods was

24   1.5 °C, while the difference in PM_{10} could reach almost 18.5 µg/m^3. The neighbourhood

25   median Ta_{max} and PM_{10} levels during "summer smog" days are shown in Figure 6. When we

26   compared mortality risks between neighbourhoods at the lowest and highest median

27   "summer smog" level (i.e. Ta_{max} 27 °C & PM_{10} 62 µg/m^3 versus Ta_{max} 28.5 °C & PM_{10} 66 µg/m^3; lag

28   2) there was a mortality risk difference of almost 3%. This difference increased up to 7% after

29   days with higher than median "summer smog" levels.

1 3.6. <u>Vulnerable groups</u>

2 The results are shown in Table 6, and reveal that mortality risk after "summer smog" days is

3 higher in very elderly people (age 85+) compared to the mortality risk in the population as a

4 whole. In the age group 65+ people who are never married or widowed seemed more

5 susceptible, while people from non-Dutch origin seemed less susceptible. Income data were

6 only available from 2003-2009. Hence, results of this sub-analysis might not be completely

7 comparable to the whole sample. Yet, the results point to a decreased risk in the highest

8 income group.

9 **4. Discussion**

10 4.1. <u>Main findings</u>

11 In this study, maximum daily air temperature was the best thermal indicator to investigate

12 heat-related mortality. We found significant effect modification of the heat-mortality

13 relationship by air pollution (PM_{10}). Stratified analyses showed that single living elderly were

14 more susceptible to heat stress than people who are younger and/or married. Mortality risks

15 varied substantially between neighbourhoods, on "summer smog" days the difference was

16 on average 3%, but could increase up to a difference of 7%.

17 The association between heat and natural-cause mortality is in line with earlier

18 studies in the Netherlands.[6,31] Huynen et al.[31] studied the impact of ambient temperature,

19 particularly the impact of heat waves and cold spells, on mortality over the period 1979-

20 1997 in the Netherlands. They found a V-like relationship between temperature and

21 mortality, with an increase in heat-related mortality of 2.72% for each degree Celsius

22 increase above 16.5 ºC. Average total excess mortality during the heat waves in the study

23 period was 12.1%. However, temperature data were derived from a single site, and the

24 mortality effects were not controlled for air pollution. Another study in the Netherlands

25 comprised the excess deaths that occurred during the hot summer (including a heat wave

26 and smog period) of 2003. Based on a quick screening the authors concluded that: "a

27 significant proportion of the deaths now being attributed to the hot summer weather can

28 reasonably be expected to have been caused by ambient ozone and, to some extent,

29 particles."[6] However, they did not specify the exact proportions caused by high

30 temperatures, by air pollution, and their interaction.

Earlier studies elsewhere also often used temperature and air quality data measured at a single site,[3] and assumed that exposure across cities is the same. This causes misclassification of exposure, and probably an underestimation of temperatures in inner-city areas. Non-differential misclassification could be more pronounced among vulnerable groups who spend more time indoors or live in areas with less thermal comfort. Effect estimates could then be biased towards the null.[3] Exposure assessment on neighbourhood level reduces the amount of misclassification. This allowed us to demonstrate that synergistic effects of heat and air pollution even occur in cities with a temperate climate and relatively low air pollution.

4.2. Limitations of the exposure assessment

Exposure assessment at the exact addresses of the cases in our study population would have been more accurate, but was not possible due to privacy regulations. Besides this limitation, there was a lack of data on behavioural and physical factors like the use of air conditioning, time spent outdoors or away from home, and the orientation, insulation and ventilation of the home that could have influenced the impact of outdoor temperature on personal exposure.

Another limitation was that a constant value of 1.2 °C was used to estimate the annual mean UHI-effect for each neighborhood. Hourly air temperatures measured at Rotterdam Airport were corrected with this annual mean UHI-effect to calculate hourly air temperatures for each neighbourhood. In reality, the UHI effect varies over time, differs between seasons, differs between day and night and also depends on the meteorological situation: air temperature, wind speed, atmospheric stability, cloud coverage. Ideally, we would have taken this into account and calculated a daily UHI-effect for each neighborhood. However, no simple parameterization yet exists that takes into account all these effects to derive a daily or hourly in-city temperature from an out-city temperature. The UHI-effect is generally largest during warm days because of more solar radiation, but can also be large during winter days because of the enhanced anthropogenic heat during winter times. The UHI-effect generally decreases for higher wind speeds, for higher cloud coverage and for stable atmospheric situations. All these effects could not be included straightforwardly.

1 ### 4.3. The use of different thermal indicators

2 By using various thermal indicators we could investigate the importance of other

3 meteorological factors in addition to temperature. Other studies have also compared

4 different thermal indices in relation to mortality, but on a less detailed level. Morabito et

5 al.[32] showed that direct multivariate indices including the effect of wind speed, solar

6 radiation, air humidity and temperature fitted best with all-cause very elderly mortality

7 attributable to heat stress. In that study, the UTCI performed best in thermal comfort

8 assessment, but was not the best predictor of mortality. A study in the Czech Republic found

9 similar heat effects on CVD mortality for air temperature and the examined thermal indices

10 (UTCI, AT and Physiologically Equivalent Temperature (PET)).[33] These studies show that there

11 is no strong evidence to favour the use of a specific thermal indicator over the use of air

12 temperature alone when studying heat-related mortality. Different thermal indicators may

13 have different impact on mortality depending on geographical context. Therefore, it seems

14 worthwhile to consider a few of them when designing heat-mortality studies. To avoid

15 multiple testing and collinearity problems, we only used Ta_{max} and PM_{10} in the multivariate

16 and interaction models.

17 ### 4.4. Susceptibility to heat-related mortality

18 As has been found in earlier studies, stratified analysis of the temperature mortality

19 association showed that the very elderly (age 85+) were more vulnerable to the effects of

20 heat and air pollution than people from younger age groups. This may be caused by a

21 weakened thermal regulatory system.[10] However, age was also associated with other

22 potentially important determinants, such as sex, ethnicity, marital status, and household

23 income. For example, the proportions of women, and of widowed people are larger in the

24 older age groups. Therefore, we also performed stratified analyses in people age 65 and

25 older. This showed slightly different results from the stratified analyses in the total

26 population. Besides the very elderly it seemed that people who are widowed or divorced or

27 with a low household income are also more vulnerable. These people may receive less social

28 attention and may have less resources to take preventive measures to cope with heat

29 stress.[1] These groups have also been mentioned by Stafoggia et al.[10] in Italy and Tian et al.[34]

30 in China. In addition, both studies mentioned people with pre-existing medical condition

31 (psychiatric disorders, depression, heart conduction disorders, circulatory disorders of the

brain), and people who reside in nursing homes or hospitals.[10,34] There was no information on those factors in our study. People from non-Dutch origin seemed less vulnerable than people from Dutch origin. This may be explained by the fact that they largely come from Turkey, Morocco and Surinam, countries with a much warmer climate than the Netherlands. These people may be more capable to acclimatize and/or adapt to higher temperatures. A limitation in our study was the incomplete household income data (only available after 2003). Hence, results regarding household income may not be completely comparable with results regarding the other susceptibility variables.

4.5. Case-crossover versus time-series studies

The advantage of the case-crossover over a time series design is that each subject serves as his or her own control. Hence, the influence of confounders that remain constant in the subject such as sex and smoking history is controlled for by design. Time-stratified selection of referent dates on the same day of the week in the same month as the case date provides adequate control for long-term trends, seasonality, day of the week and month. Potential interaction between exposures can be assessed at individual rather than at the group level.[23,24] In addition, an issue in time-series studies is that the composition and size of the total population at risk may vary because of the effects of prior exposures, which might happen when after the first warm days very frail individuals are affected earlier than others ("harvesting effect"). In that case, positive associations found over the first warm days might be offset by negative associations over the subsequent warm days.[3] This problem is avoided when using a case-crossover design, because exposure and event are assessed at the individual level rather than at the population level.[25]

5. Conclusions

We found significant synergistic effects of high temperatures and air pollution on natural-cause mortality in a city with a temperate climate. Single living elderly are the most vulnerable group. Due to the urban heat island effect and spatial differences in air pollution levels, mortality risks vary substantially between neighbourhoods, with a difference up to 7%.

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7. Tables

2

3 Table 1. Demographic characteristics of the study population

Case characteristics	Total	Age ≥ 65 years
Natural-cause mortality cases (absolute n over 1995-2009)	73,178	60,407
Age category (n, (%))		
<45 years	2,679 (3.7)	-
45-64 years	10,092 (13.8)	-
65-84 years	36,339 (49.7)	36,339 (60.2)
≥85 years	24,068 (32.9)	24,068 (39.8)
Sex (n, (%))		
Male	33,816 (46.2)	26,088 (43.2)
Female	39,362 (53.8)	34,319 (56.8)
Ethnicity (n, (%))		
Dutch origin	62,766 (85.8)	54,349 (90.0)
Western origin	5,168 (7.1)	3,880 (6.4)
Non-western origin	5,208 (7.1)	2,177 (3.6)
Marital status (n, (%))		
Never married	8,461 (11.6)	4,976 (8.2)
Married	25,936 (35.4)	20,377 (33.7)
Widowed	29,866 (40.8)	29,258 (48.4)
Divorced	8,915 (12.2)	5,796 (9.6)
Household income[a] (n, (%))		
cat1 (<14842 €/year)	13,853 (52.5)	11,856 (54.1)
cat2 (14842-19850 €/year)	7,014 (26.6)	5,980 (27.3)
cat3 (19850-26497 €/year)	3,311 (12.6)	2,497 (11.4)
cat4 (>26497 €/year)	2,203 (8.4)	1,599 (7.3)

4 a. Standardised household income, corrected for differences in size and composition of the household.

5

1   Table 2. Correlation between the various thermal and air pollution indices during the study
2   period

	Ta_{max}	$Tmrt_{max}$	$UTCI_{max}$	PM_{10}	NO_2	O_3
Ta_{max}	1.00					
$Tmrt_{max}$	0.78	1.00				
$UTCI_{max}$	0.91	0.92	1.00			
PM_{10}	-0.02	-0.02	0.02	1.00		
NO_2	-0.26	-0.22	-0.17	0.48	1.00	
O_3	0.63	0.70	0.64	-0.12	-0.40	1.00

3   Ta_{max}: daily maximum air temperature, $Tmrt_{max}$: daily maximum mean radiant temperature, $UTCI_{max}$: daily
4   maximum Universal Thermal Comfort Index, PM_{10}: particulate matter with diameter of 10 micrometers or less,
5   NO_2: nitrogendioxide, O_3: ozone
6

1 Table 3. Percentage risk increase of natural-cause mortality for an increase between the 90
2 and 99% of the thermal index at different lag times, derived from univariate conditional
3 logistic regression models

Parameter	Lag	90-99%	% risk increase	p-value	AIC
Ta_{max}	0	23.3-30.1	9.3	<0.01	215953
$Tmrt_{max}$	0	55.8-61.9	2.6	<0.01	215974
$UTCI_{max}$	0	31.6-37.6	6.4	<0.01	215960
Ta_{max}	1	23.3-30.1	10.6	<0.01	215899
$Tmrt_{max}$	1	55.8-61.9	4.0	<0.01	215903
$UTCI_{max}$	1	31.6-37.6	7.5	<0.01	215901
Ta_{max}	2	23.3-30.1	9.2	<0.01	215806
$Tmrt_{max}$	2	55.8-61.9	2.7	<0.01	215819
$UTCI_{max}$	2	31.6-37.6	6.2	<0.01	215808

4

1   Table 4. Percentage risk increase of natural-cause mortality per iqr increase in air pollution
2   parameter at different lag times, derived from univariate conditional logistic regression
3   models

Parameter	Lag	Median (IQR)	% risk increase	95% CI	AIC
PM$_{10}$	0	31.8 (20.8)	1.7	(0.8-2.6)	215973
NO$_2$	0	38.3 (19.9)	1.1	(-0.3-2.4)	215983
O$_3$	0	42.0 (34.6)	2.9	(1.1-4.7)	215974
PM$_{10}$	1	31.8 (20.8)	1.6	(0.6-2.5)	215925
NO$_2$	1	38.3 (19.9)	0.5	(-0.4-1.4)	215927
O$_3$	1	42.0 (34.6)	3.4	(1.6-5.3)	215923
PM$_{10}$	2	31.8 (20.8)	1.2	(0.2-2.1)	215827
NO$_2$	2	38.3 (19.9)	1.7	(0.4-3.1)	215827
O$_3$	2	42.0 (34.6)	1.4	(-0.4-3.2)	215831

4

5

1　Table 5. Number of days with a certain temperature and air quality combination during
2　study period (when $Ta_{max} \geq 15ºC$) (n (%))

Ta_{max}	PM$_{10}$ <15 µg/m³	15-30 µg/m³	30-50 µg/m³	50-70 µg/m³	>70 µg/m³	Total
15 – 19 ºC	30 (1.1)	730 (27.3)	423 (15.8)	111 (4.1)	51 (1.9)	1345 (50.2)
20 – 24 ºC	6 (0.2)	377 (14.1)	400 (14.9)	140 (5.2)	38 (1.4)	961 (35.9)
25 – 29 ºC	0 (0.0)	53 (2.0)	135 (5.0)	79 (3.0)	46 (1.7)	313 (11.7)
30 – 36 ºC	0 (0.0)	6 (0.2)	21 (0.8)	14 (0.5)	19 (0.7)	60 (2.2)
Total	36 (1.3)	1166 (43.5)	979 (36.5)	344 (12.8)	154 (5.8)	2679 (100.0)

3

1 Table 6. Percentage risk increase of natural-cause mortality on "summer smog" days (Ta_{max}

2 25 ºC; PM_{10} 50 $\mu g/m^3$) (lag 2) stratified for potentially vulnerable groups in the total

3 population and in the population aged 65 or older

| Substrata	Total population	Population aged 65+
	% risk increase 95% CI	% risk increase 95% CI
Age category (n, (%))		
<45 years	7 (6-9)	-
45-64 years	8 (7-9)	-
65-84 years	6 (5-6)	-
≥85 years	10 (9-11)	-
Sex (n, (%))		
Male	8 (7-8)	8 (7-8)
Female	7 (7-7)	7 (7-8)
Ethnicity (n, (%))		
Dutch origin	8 (7-8)	8 (7-8)
Western (non-Dutch) origin	5 (4-7)	6 (4-8)
Non-western origin	8 (7-10)	4 (2-6)
Marital status (n, (%))		
Never married	9 (8-10)	9 (7-10)
Married	7 (6-7)	5 (4-6)
Widowed	10 (9-10)	9 (9-10)
Divorced	1 (0-2)	3 (2-4)
Household income (n, (%))		
cat1 (<14842 €/year)	12 (10-13)	15 (14-17)
cat2 (14842-19850 €/year)	14 (11-15)	11 (9-13)
cat3 (19850-26497 €/year)	17 (14-20)	20 (16-24)
cat4 (>26497 €/year)	1 (-3-5)	-3 (-7-1)

4

1 **8. Figures**

2
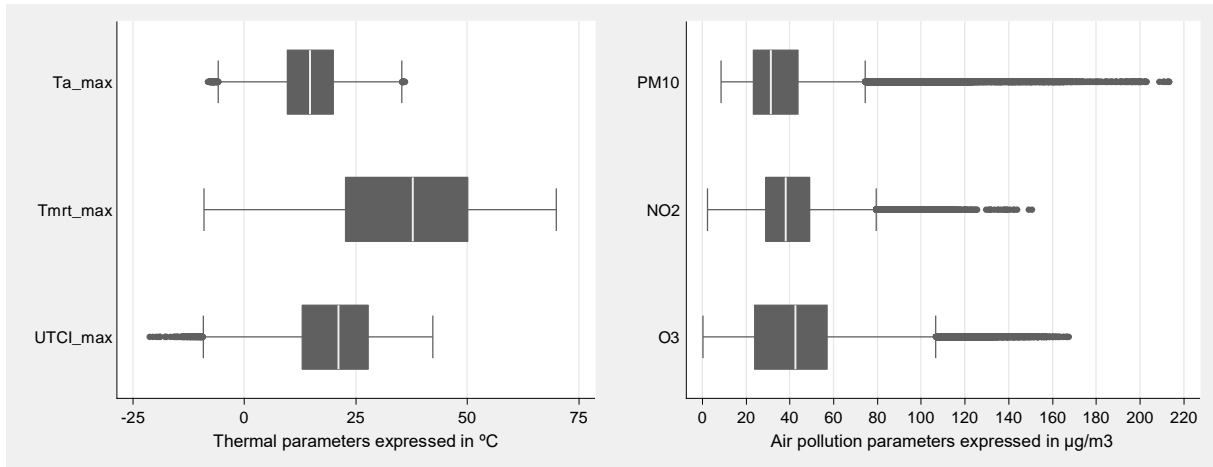
3

4 Figure 1. Distribution of thermal and air pollution exposure during the study period

5 Ta$_{max}$: daily maximum air temperature, Tmrt$_{max}$: daily maximum mean radiant temperature, UTCI$_{max}$: daily
6 maximum Universal Thermal Comfort Index, PM$_{10}$: particulate matter with diameter of 10 micrometers or less,
7 NO$_2$: nitrogendioxide, O$_3$: ozone
8
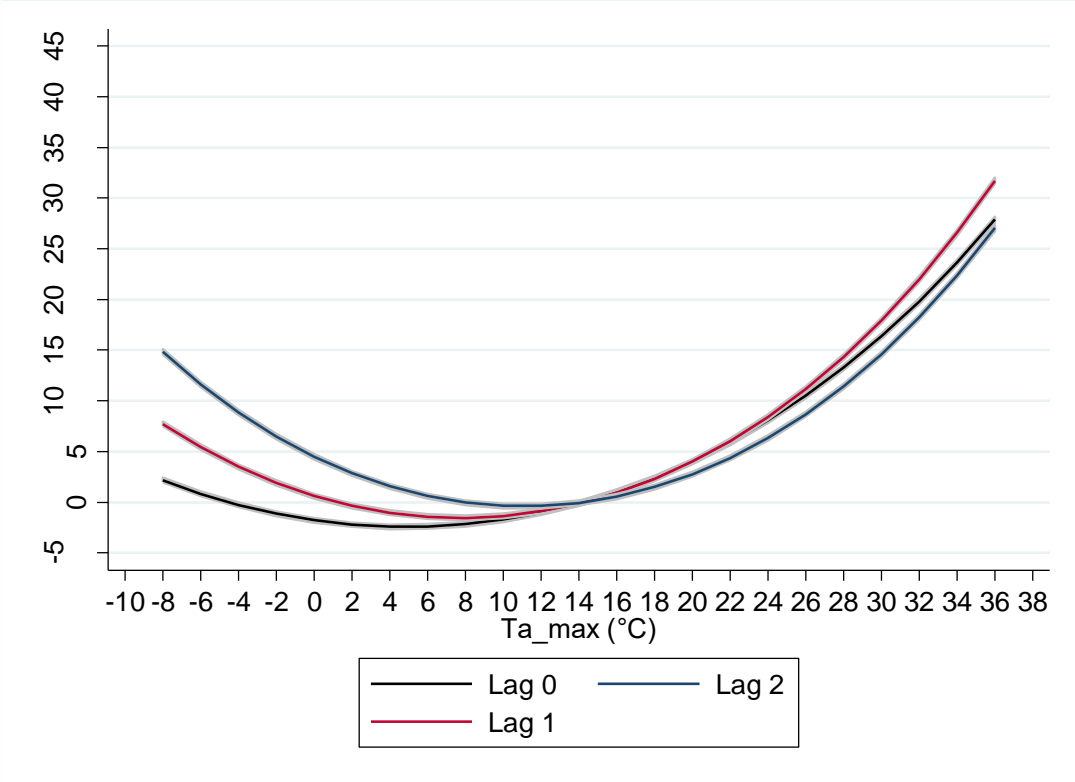
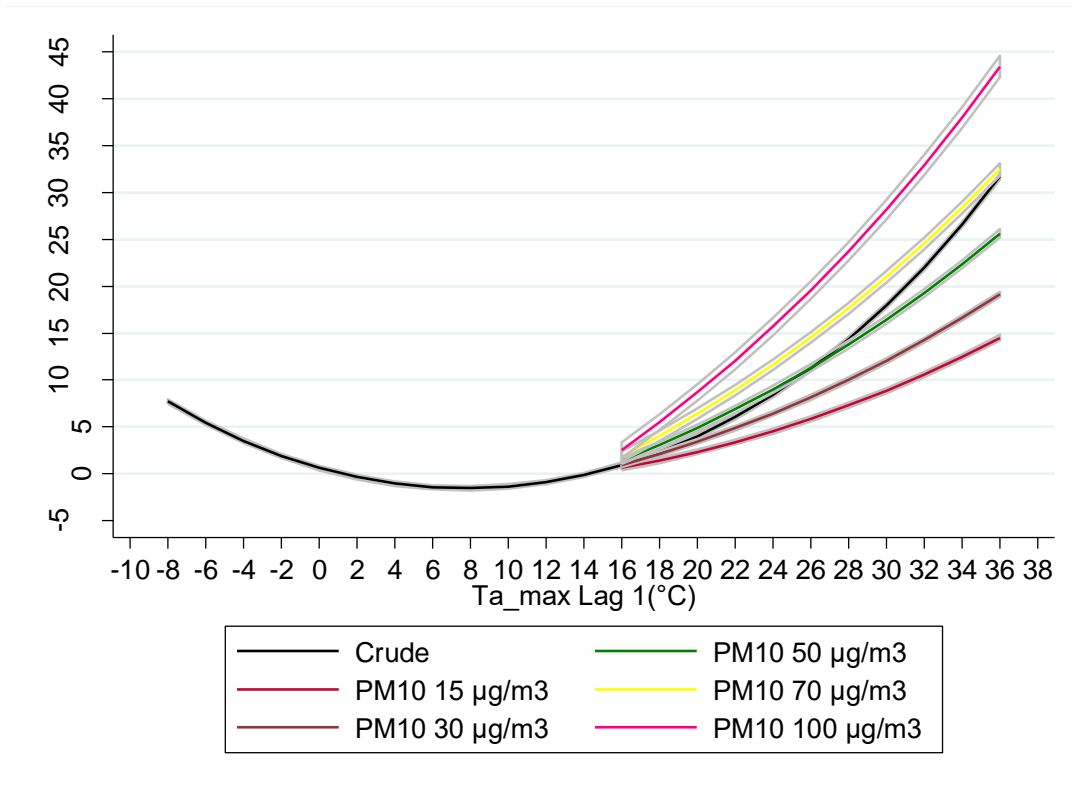Figure 2. Univariate association between Ta_{max} and natural-cause mortality at different lag times.
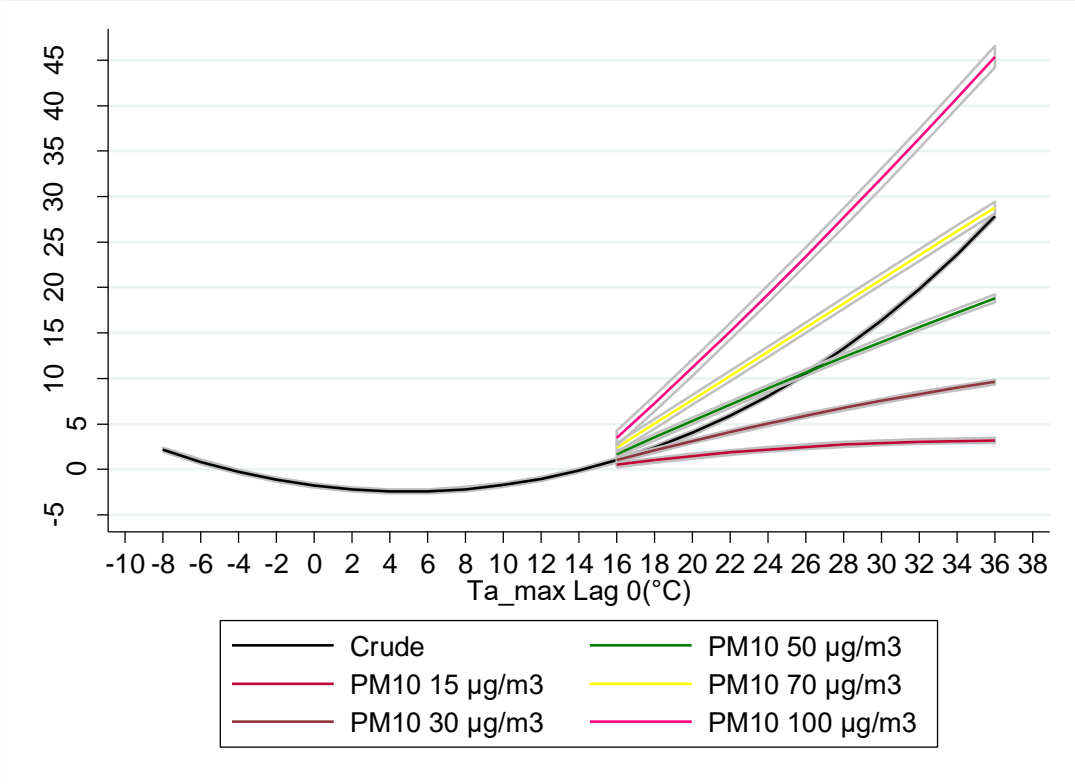
Figure 3. Interaction between Ta_{max} and PM_{10} of the effect on natural-cause mortality at lag 0 (AIC 215942).

1
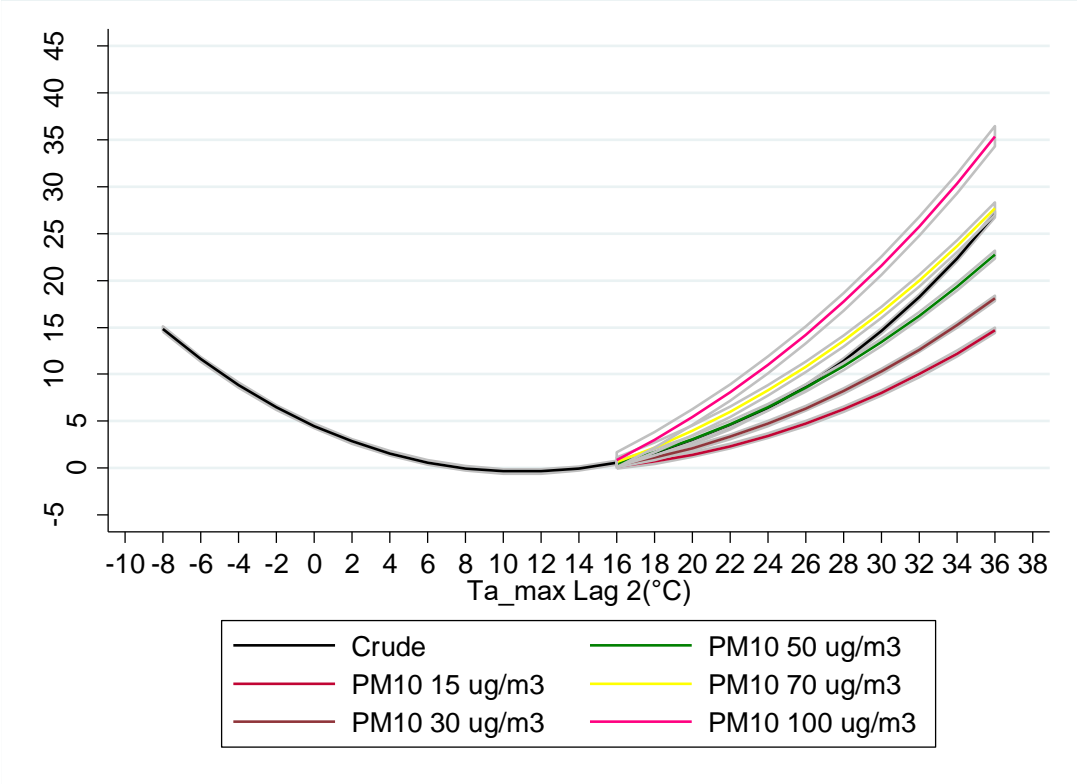

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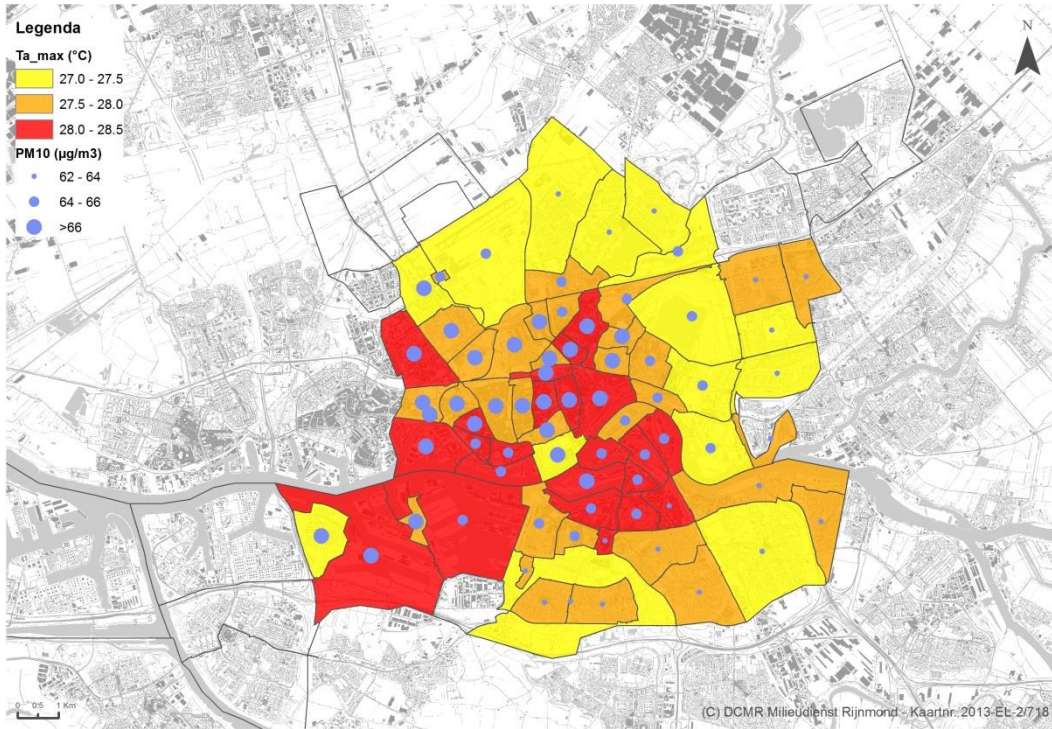
3 Figure 4. Interaction between Ta_{max} and PM_{10} of the effect on natural-cause mortality at lag
4 1 (AIC 215896).

5

Figure 5. Interaction between Ta_{max} and PM_{10} of the effect on natural-cause mortality at lag 2 (AIC 215806).

1

2   Figure 6. Median Ta$_{max}$ and PM$_{10}$ levels during "summer smog" d